Response to October 12, 2005, Office Action Atty Dkt No. 02-0175 Application No. 10/729,499

Please delete the second Example 4 beginning on page 55 and replace Example 5 with the following text. A marked-up version of the specification indicating the amendments made herein is presented in Appendix A.

EXAMPLE 5

Preparation of a Compound of Formula I in which A is CH_2 , R^1 is 2,6-Dimethylphenyl, R^2 is 2-Methylbenzothiazol-5-yl, R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , and R^{21} are Hydrogen, T is Oxygen, X^1 is a Covalent Bond, and Y is $-CH_2CH_2$ -

- A. To a mixture of N-(2,6-dimethylphenyl)-3-bromopropanamide (1g, 4.5 mmol) and N-carbobenzyloxypiperazine (1,7g, 6.8 mmol) in 10 mL of acetone was added potassium carbonate (0.93 g, 6.8 mmol). The mixture was refluxed for 24 hours. The mixture was filtered, and the solvent was removed from the filtrate under reduced pressure. The residue was purified using column chromatography, to provide N-(2,6-dimethylphenyl)-3-(4-carbobenzyloxypiperazinyl)propanamide, a compound of formula (3).
- B. To N-(2,6-dimethylphenyl)-3-(4-carbobenzyloxypiperazinyl)propanamide (1.3g) in 10 mL of methanol was added 10% Pd/C, and the mixture was hydrogenated at 30 psi for 24 hours. The mixture was filtered, and the solvent was removed from the filtrate under reduced pressure, to afford N-(2,6-dimethylphenyl)-3-piperazinylpropanamide, a compound of formula (4), which was used without further purification.
- C. A mixture of N-(2,6-dimethylphenyl)-3-piperazinylpropanamide (0.15 g, 0.57 mmol) and 2-methyl-5-(oxiran-2-ylmethoxy)benzothiazole (0.127 g, 0.57 mmol) in 8 mL of ethanol was refluxed for 24 hours. The solvent was removed under reduced pressure, and the residue was purified using preparative TLC.

Response to October 12, 2005, Office Action Atty Dkt No. 02-0175 Application No. 10/729,499

D. Preparation of Other Compounds of Formula I

Similarly, following the procedure of 5A above, but optionally replacing N-(2,6-dimethylphenyl)-3-piperazinylpropanamide with other compounds of formula (4), and optionally replacing 2-methyl-5-(oxiran-2-ylmethoxy)benzothiazole with other compounds of formula (5), the following compounds of Formula I were prepared:

3-{4-[(2S)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-(2,6-dimethylphenyl)propanamide;

N-(2,6-dimethylphenyl)-3-{4-[2-hydroxy-3-(2-methoxyphenoxy)-propyl]piperazinyl}propanamide; and

3-{4-[(2S)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]-2,5-dimethylpiperazinyl}-N-(2,6-dimethylphenyl)propanamide.

E. <u>Preparation of Other Compounds of Formula I</u>

Similarly, following the procedure of 5C above, but optionally replacing N-(2,6-dimethylphenyl)-3-piperazinylpropanamide with other compounds of formula (4), and optionally replacing 2-methyl-5-(oxiran-2-ylmethoxy)benzothiazole with other compounds of formula (5), other compounds of Formula I are prepared: